Multi-resolution three-dimensional multi-modality Image Registration by Maximization of Mutual Information

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Abstract-**Maximization of mutual information is a very powerful criterion for 3D medical image registration, allowing robust and accurate fully automated rigid registration of multi-modal images in a various applications. In this paper, we presented a method based on normalized mutual information with sub-sampling of the images for 3D image registration on the images of CT, MR and PET. Powell's direction set method and Brent's one-dimensional optimization algorithm were used as optimization strategy. A multi-resolution approach was applied to speedup the matching process. For PET images, pre-processing of segmentation was performed to reduce the background artifacts. According to the evaluation by Vanderbilt University, the average of mean of registration error for CT-MR task was 1.47 mm and for MR-PET task was 3.22 mm. The registration images with edge extraction showed good matches by visual inspection. Sub-voxel accuracy in multi-modality registration had been achieved with this algorithm.**

I. Introduction

Imaging registration is a prerequisite to medical imaging. Each imaging modality provides different and useful information. Anatomical modalities depict primarily morphology, such as X-ray, CT (Computed Tomography)，MRI (Magnetic Resonance Imaging), US (Ultrasound), acquired by various image systems. Functional modalities depict primarily information on the metabolism but have no enough information about anatomy, including γ camera, SPECT (Single Photon Emission Computed Tomography), PET (Positron Emission Tomography). Since information obtained from different time on same modality or multiple modalities is usually of a complementary nature, proper registration is desired in clinical diagnoses, radiotherapy planning and surgical evaluation.

There are two kinds of multi-modality image registration methods—extrinsic method and intrinsic method [1,2,3,4]. The former is used usually as gold standard for registration evaluation. The later only relies on patient generated image content. Maximization of mutual information has been recommended as a powerful intrinsic criterion for multi-modal medical image registration. The method applies the concept of mutual information to measure the statistical dependence between the image intensities of corresponding voxel in both images, which is assumed to be maximal if the images are geometrically aligned.

In this paper, we presented a method based on normalized mutual information with sub-sampling of the images for 3D image registration of CT, MR and PET. Powell's direction set method and Brent's one-dimensional optimization algorithm were used as optimization strategy. For PET

images, pre-procession of segmentation was performed to reduce the background artifacts. The accuracy was validated to be sub-voxel by comparing to the stereotactic registration solution according to the evaluation by Vanderbilt University.

II. Methodology

A. Image Acquisition

The raw data of images of 18 patients were provided by the project of Vanderbilt University, entitled "Evaluation of Retrospective Image Registration". In each data set from patient_001 to patient_009, there were one CT data and/or one PET data, and six MR data (PD, T1, T2, PD_rectified, T1_rectified, T2_rectified), which were all low resolution images. From patient_101 to patient_109, the following four image volumes of high resolution were included: one axial CT and three axial MR Spin-Echo (PD, T1 and T2) images.

An overview of the resolution of the data sets could be found in Table I. The raw data were encoded as two-byte two's complement integers. The byte order was BigEndian. All data sets were normalized to the range of 0~255 for processing.

B. Pre-processing of PET Images

As blurs occurred in PET images, the PET images were pre-segmented to reduce the radiated artifacts [5].

C. Sub-sampling and Mutual Information [6,7,8]

One of the images was selected as a floating image F and another to be a reference image R. Rigid body transformation was applied for multi-modal images of head because it is reasonable to assume that bone of the skull is rigid. The transformation was restricted to six degrees of freedom (three translations and three rotations), thus:

$$V_R \cdot (P_R - C_R) = R(\phi_x) \cdot R(\phi_y) \cdot R(\phi_z) \cdot V_F \cdot (P_F - C_F) + t(t_x, t_y, t_z) \quad (1)$$

where V was a 3*3 diagonal matrix representing the respective voxel size, P was the orientation of the respective image, C was the image center, R was the rotation around three axis, ϕ was the rotation angle and t was the translation vector.

The images were not pre-registered other than having their centers aligned and their axes orientation corresponding. Samples were taken from F on a regular grid at different sample intervals in the x, y and z direction respectively and transformed by the geometric transformation into the reference image R. Then the joint and marginal histograms of the intensities f and r of corresponding voxels in the volume

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Abstract

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of overlap of *F* and *R* were constructed and from which the normalized mutual information registration criterion *ECC(F,R)* was computed.

The sampling range was chosen to be within a 20cm*20cm square around the centers. The equidistant sampling was controlled by sampling factors: setting a sampling factor to a positive integer x resulted in only one out of every x voxels along an image axis being used in the computation. The sampling factors were defined separately for each dimension corresponding to experience. The high resolution images were sub-sampled with a factor of 3 in plane and 1 out-of-plane. The low resolution images were matched in a coarse-to-fine manner and two layers were used. The low resolution images were sampled in plane by factors 3 and out-of-plane by factors 1 in the first level and by factor 1 in each dimension in the second level.

If the corresponding point for one sample after transformation was outside the reference image, the intensity would be defined to be equal to that of its nearest neighbor on the volume edge.

In most cases, the transformed position of a voxel in *F* was not coincided exactly with a voxel position in *R*. Therefore, interpolation was required. Our choice was cubic spline interpolation method.

With the normalized mutual information of two images (A and B), the Entropy Correlation Coefficient(ECC), was defined in terms of the entropies H(A) and H(B) of the images, combined with their joint entropy H(A,B) [9,10], as follows:

$$ECC(A,B) = \frac{2\big(H(A)+H(B)-H(A,B)\big)}{H(A)+H(B)} \qquad (2)$$

and

$$H(A) = -\sum_{k=1}^{n} p_k \log p_k \qquad (3)$$

D. Optimization Strategy

The six parameters were optimized by Powell's multi-dimensional direction set method, combined with Brent's one-dimensional optimization algorithm to maximize $ECC(F,R)$. The initial values of all parameters were set to zero, and the initial direction matrices were set to unit vectors. The best searching sequence of parameters was proved to be $(t_x, t_y, \phi_z, \phi_x, \phi_y, t_z)$.

E. Evaluation Method

There was no really a "gold standard" for accuracy of medical image registration, but a prospective method based on fiducial markers could be taken as a "gold standard" to perform an objective, blinded evaluation of the accuracy of retrospective image-to-image registration techniques. Image volumes of three modalities(CT, MR and PET) were taken of patients undergoing neurosurgery at Vanderbilt University Medical Center. These volumes had all traces of the fiducial markers removed, and were provided to project collaborators outside Vanderbilt, who performed retrospective registrations

on the volumes, calculating transformations from CT to MR and/or from PET to MR, and communicated their transformations to Vanderbilt where the accuracy of each registration was evaluated. In the evaluation, the accuracy was measured at multiple "regions of interest", i.e. areas in the brain which would commonly be areas of neurological interest. A region was defined in the MR image and its centroid C was determined. The prospective registration was used to obtain the corresponding point C′ in CT or PET. To this point the retrospective registration was then applied, producing C″ in MR. Statistics were gathered on the target registration error, which was the disparity between the original point C and its corresponding point C″.

This study was carried out in a blinded fashion, in the sense that the investigators at sites outside Vanderbilt did not know the standard results and the researchers did not know the exact registration algorithm.

TABLE I
DESCRIPTION OF THE IMAGE VOLUMES

Modality	Voxel Dimensions	Image Dimensions (mm)	Data Range (approx)
Low resolution:			
CT	512^2*[28~34]	0.65^2*4.0	-1024~2000
MR	256^2*[20~26]	$[1.25~1.28]^2$*[4.0~4.16]	0~2000
PET	128^2*15	2.59^2*8.0	-128~1200
High resolution:			
CT	512^2*[40~49]	$[0.40~0.45]^2$*3	-1024~2000
MR_PD	256^2*[51~52]	$[0.78~0.86]^2$*3	0~4000
MR_T1	256^2*52	$[0.78~0.86]^2$*3	0~4000
MR_T2	256^2*52	$[0.78~0.86]^2$*3	0~4000

III. RESULTS

Our registration results were shown in table Ⅱ and table Ⅲ which had been evaluated by Vanderbilt University.

TABLE Ⅱ
THE REGISTRATION ERROR OF CT-MR (unit: mm)

	CT-PD	CT-T1	CT-T2	CT-PDr	CT-T1r	CT-T2r
mean	2.28	1.73	2.20	0.78	0.78	1.04
SEM	0.08	0.06	0.94	0.07	0.06	0.09
SD	0.77	0.77	1.15	0.52	0.42	0.72

TABLE Ⅲ
THE REGISTRATION ERROR OF PET-MR (unit: mm)

	PET-PD	PET-T1	PET-T2	PET-PDr	PET-T1r	PET-T2r
mean	4.68	3.54	3.27	2.36	2.42	3.02
SEM	0.40	0.27	0.19	0.19	0.18	0.29
SD	2.91	2.13	1.51	1.29	1.12	2.02

*

Since the voxel sizes of images F and R were different, a virtual voxel size was defined for compare. If the registration error was smaller than the virtual voxel size, the registration accuracy was sub-voxel. The length of diagonal of MR was defined when CT and MR were matching and that of PET was defined when PET and MR were matching as the size of the virtual voxel. That was,

$$\sqrt{1.25^2 + 1.25^2 + 4.0^2} \approx 4.373 \,(mm) \text{ and}$$

$$\sqrt{2.59^2 + 2.59^2 + 8.0^2} \approx 8.80 (mm) \text{ for each case. In table } \mathrm{II}$$

and table Ⅲ, the mean error and SD were far smaller than the respective virtual voxel size.

IV. DISCUSSION

Practice data set and the standard results of which were provided by Vanderbilt University for mistake checking. It had been used for some experiments and visual inspection in registration.

A. Embedding of Mutual Information

We used both standard formulation of mutual information and a normalized form. It was shown in our experiment that both performed fairly well, but it seemed that higher accuracy was achieved with normalized mutual information. So the normalized form was used for all the data.

B. Sub-sampling and Multi-resolution

The whole image was chosen to be the sampling range and the result showed that the accuracy was not as high as expected. It might due to the partial volume effect and the participation of background artifact, which caused local optimum of mutual information. It was better to choose the range described in the methodology section. The sub-voxel registration had been achieved in the first layer of the pyramid. Pluim et.al showed that the accuracy of the multi-resolution matching was not significantly improved than that of direct registration as observed in our experiment. But it reduced the computation time. For that reason, the multi-resolution strategy was chosen.

C. Pre-processing

The results showed that when the PET images were not pre-segmented, the registration error was sub-voxel, but was bigger than that achieved by pre-segmented PET.

V. CONCLUSION

Our results demonstrated that sub-voxel multi-modal registration accuracy had been achieved using the maximization of normalized mutual information, which made this method suited for clinical applications.

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